**Title**: [title]

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1 Afiliación, lugar.

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## Abstract

**Objective**: […]. **Material and methods**: […]. **Results**: […]. **Conclusion**: […].

**Keywords**: […].

# Introduction

[…].

[…].

[…].

# Material y methods

## Participants

[…].

## Instruments

### Instrument 1

[…].

### Instrument 2

[…].

## Procedures

[…].

[…].

## Statistical analysis

Data is presented as median (*Mdn*) and interquartile range (*IQR*) for continuous variables; for categorical/discrete variables, the absolute and relative sample size was reported.

A non-parametric approach was used since the underlying distribution of continuous measured outcomes, assessed through analytical and graphical methods, did not follow a Gaussian distribution.

In order assess the differences in developmental scores between males and females, the *Wilcoxon* rank-sum test was used, meanwhile the chi-square test () was used to evaluate the goodness-of-fit () and the independence of factors ().

Generalized additive models (GAM) were used to describe linear and non-linear relationships in the form of smooth terms between developmental characteristics, represented through penalized regression splines ([1](#ref-wood2011fast)). Restricted maximum likelihood (i.e., REML) method was used for the estimation of the smoothing parameters, and thin-plate regression splines for smoothing basis, as they are the optimal smoother of any given basis dimension/rank ([2](#ref-wood2003thin)). To describe the smooth terms by means of quasi-linear segments, we used approximative effect derivatives to summarise the trend with 95% confidence intervals.

To account for any source of variability coming from subject’s sex, evaluators and the type of relationship between the infants with the respondents, we incorporate them as random effects in the fitted models in the form of penalized parametric terms ([3](#ref-wood2016smoothing)).

A probability of committing a type I () error of less than 5% (*p* < 0.05), was considered sufficient evidence for statistical significance in hypothesis testing. All the statistical analyses were computed and implemented in the R programming language ([4](#ref-rlanguage)). GAMs and the corresponding model estimates were computed using the *mgcv* and *modelbased* packages with their corresponding documentation ([5](#ref-wood2017generalized),[6](#ref-dominique2020estimation)). Complementary R packages were used for visualization purposes ([7](#ref-hadley2016ggplot2),[8](#ref-daniel2021see)).

# Results

From a total of 234 subjects with congenital hypotonia, 94 (40.2%) were females and 140 (59.8%) males ( (1) = 9.04, *p* = 0.003, = 0.19, CI0.95%[0.09, 1]). The developmental characteristics of the sample can be seen in [Table 1](#tab1).

When modelling the effect of chronological age corrected for prematurity on developmental domains, we observed a significant non-linear relationship on communication scores ( (5.2, 224.04) = 13.43, *p* < 0.001), that reflect an overall negative marginal effect ( = -2.36, CI95%[-3.47, -1.25], (224.04) = -4.2, *p* < 0.001), however, this was not true when assessing the direction of the effect in the age range between 1 to 7 ( = 0.49, CI95%[-0.89, 1.86], (224.04) = 0.45, *p* = 0.319), and neither in the 18 to 48 months old group ( = 0.45, CI95%[-1.32, 2.23], (224.04) = 0.42, *p* = 0.593), whereas the effect tend to be positive but non-significant.

When analysing the motor skills domain, we found a significant non-linear effect of corrected age on gross motor scores ( (5.24, 226.75) = 6.19, *p* < 0.001), which had an overall positive effect ( = 1. 95, CI95%[0.66, 3.25], (226.75) = 2.97, *p* = 0.003), however, the slope varied as a function of age, with a negative effect on gross motor score = -2.94, CI95%[-4.55, -1. 34], $ (226.75) = -3.7, *p* = 0.004, but in the range 9.7 to 15.5 a positive effect was observed ( = 1.86, CI95%[0.61, 3.11], (226.75) = 2.93, *p* = 0.009), while in the range 7.3 to 9.2 ( = 0.02, CI95%[-1. 12, 1.17]) and 16 to 48 months ( = -0.02, CI95%[-2.05, 2.01]) the slope was non-significant and virtually zero ( (226.75) = 0.06, *p* = 0.45, and (226.75) = 0.07, *p* = 0.646 respectively).

The relationship between developmental domains and corrected age can be seen in [Figure 1](#fig1).

# Discussion

[…].

[…].

[…].

# Conclusion

[…].

# Acknowledgment

[…].

# Conflicts of interest

[…].

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**Table 1**. Overall baseline and developmental characteristics of the sample and grouped by sex. 1 Data is presented as sample size, and *Mdn* (*IQR*); 2 P-values derived from the *Wilcoxon* rank-sum test.

**Figure 1**. Relationship between corrected age (in months) and developmental domains. Regression lines and shaded area represent predicted values estimated from GAM models and their 95% confidence interval. Points and error bars represent the mean and standard error at 5-month age intervals.